EXHIBIT 28

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Dear Mr. Moriarty,

My name is Lewis P. Amsel, Ph.D. and I am the President of Pharmaceutical Consulting Services, Inc.

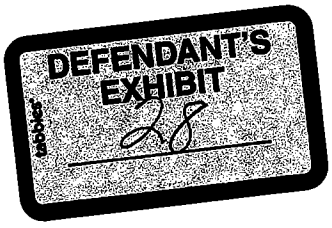
You have retained me to review certain documents related to the Digitek litigation. These documents relate to the manufacturing process, testing, packaging, stability and cGMP processes of Digitek. More specifically, I have been engaged to evaluate issues relating to "double thick" Digitek tablets and "variable dose" Digitek tablets.

I have reviewed numerous documents for my report; a listing appears in the Appendix. My conclusions are that the Digitek process was robust in that the blending operation and subsequent tabletting consistently produced tablets that met specifications. Furthermore, there is no evidence that a patient ever received a "double thick" tablet.

A synopsis of my background in the pharmaceutical sciences follows:
B.Sc. in Pharmaceutical Sciences, Columbia University
Ph.D. in Pharmaceutical Sciences, State U of NY at Buffalo (Thesis: Factors Influencing the Conjugation of Drugs with Glycine, major professor: Dr. Gerhard Levy).

In 2006, I formed Pharmaceutical Consulting Services, Inc (PCS). to provide support to emerging and established pharmaceutical companies in the areas of product formulation, development, and to support interaction with contract manufacturers for scale up and production. PCS also provides support in the preparation of Chemistry, Manufacturing and Control (CMC) sections of Investigational New Drug (IND) applications, New Drug Application (NDA) submissions, Abbreviated New Drug Applications (ANDA), patent review and support for formulation issues, optimization of manufacturing processes and implementation of "right first time" practices.

Previously, I was Vice President, Pharmaceutical Technology at Watson Pharmaceuticals. Prior to joining Watson, I was Executive Director of Worldwide Pharmaceutical Technology for Searle Corp., subsequently Pharmacia Inc. and finally Pfizer Inc. I was Assistant Vice President of R&D at R.P. Scherer Corp. and Director of the Pharmaceutical and Analytical Division at Pennwalt Corp. I also held the position of Adjunct Assistant Professor at SUNY Buffalo from 1979-1986. My career in the pharmaceutical industry encompasses more than 35 years in managerial positions of R&D and Manufacturing.



Manufacture of Digitek Tablets
Overview of Process:

Digitek was manufactured by a direct compression process. This method of tablet manufacture blended the requisite powder ingredients in the appropriate proportions. This blend, when compressed on a rotary tablet press produced satisfactory tablets.

A. **Ingredients and Purpose**:

Below is a list of ingredients used in the manufacture of Digitek and their purpose (Ref: [1]):

Corn Starch, NF: Used as an ingredient to assist in tablet disintegration and dissolution.

Digoxin, Micronized, USP: Active pharmaceutical ingredient.

D & C Yellow #10, Aluminum Lake: Colorant, (Contained in .125mg tablet).

Croscarmellose Sodium, NF: Used as an ingredient to assist in tablet disintegration and dissolution.

Lactose Hydrous, Impalpable, NF: Tablet diluent.

Starch, Pregelatinized, NF: Tablet disintegrant.

Microcrystalline Cellulose 101, NF: Tablet binder, used to hold materials in a cohesive form after compression.

Lactose Anhydrous, DT, NF: Tablet binder.

Stearic Acid, NF: Tablet lubricant, to aid in ejection of tablet from the die.

Silicon Dioxide, NF: Glidant, to aid the flow of the powder blend in the tablet press hopper.

These ingredients when combined in the appropriate proportions and blended can be compressed into tablets using standard tablet press equipment such as the Stokes BB2-45.

B. **Processing:**

All ingredients that were used in preparing Digitek tablets were assayed and released as per approved specifications by Quality Control (QC) before processing into Digitek.

All calculations used to determine input quantity of digoxin and excipients as delineated in the Master Batch Record and the approved ANDA were performed by one individual and checked for accuracy by a second individual. Additionally, inventory control acted as a secondary check on the correct input of active drug and excipients.

All label checking was performed by one person and checked by another person. This process was performed to ensure that the correct ingredient was incorporated into the batch to be manufactured.

All utensils, scales, processing rooms, blenders, tablet presses, etc. were inspected for cleanliness by one person and approved by a second person from Quality Assurance (QA).

1. Weighing:

Digitek tablets were made in 3 separate parts of identical composition which were combined prior to final blending and tabletting. Each ingredient was weighed into 3 separate containers each containing 1/3 of the total to be used.

Stearic acid and silicon dioxide were not divided into thirds as they were added into the final blend. Addition of lubricant and glidant into the final blend, followed by brief mixing is routine in tablet manufacture to prevent "over lubrication" which can impair tablet dissolution.

Each ingredient was weighed by one person and checked by a second person to ensure the correct ingredient as well as the correct amount was added. This is standard practice to eliminate errors. My review of numerous batch records indicated that all data recorded for weights were consistent with the Master Batch Record (Ref: [3]).

2. Blending:

The blending of ingredients in the manufacture of Digitek proceeded by geometric dilution. This sequential blending of ingredients (in which greater amounts are progressively added) ensured satisfactory and even distribution of digoxin throughout the batch. Some of the ingredients were screened before addition to the blender to break up any lumps that may have been present in the manufacturer's bulk container.

Step 1:
Corn Starch, Digoxin, D&C Yellow #10 Aluminum Lake (.125mg. tablet only) and Croscarmellose Sodium were added into a 3 cubic ft. twin shell blender with intensifier bar and blended for 10 minutes with the intensifier bar "on". The intensifier bar provided additional agitation and enhanced mixing. The twin shell blender (also referred to as a "V" blender) is a highly efficient blender with proven performance in the pharmaceutical industry for many years. Each rotation of the blender about its axis divides the powder bed in half and then recombines the powder bed. Typically, this type of blender will rotate at 15-25 RPM.

Step 2:
To the blender, Lactose Hydrous Impalpable was added and blended for 10 minutes with the intensifier bar "on" and an additional 10 minutes with the intensifier bar "off".

The blend was discharged into drums labeled appropriately as Parts 1, 2, 3 (each part being 1/3 the total).

Step 3:
Each part was then added separately into the 10 cubic ft. twin shell blender.
Starch, Pregelatinized and Microcrystalline Cellulose were added into the blender and blended for 10 minutes with the intensifier bar "off".

Step 4:
Lactose, Anhydrous DT was added to the blender and blended for 10 minutes with the intensifier bar "on" and 10 minutes with the intensifier bar "off".

The blend was discharged in separate containers appropriately labeled Parts 1, 2, 3.

Step 5:
Blended material from Step 4 (all 3 parts) was added into the 50 cubic ft. double cone blender. The operation principle of this blender is similar to the twin shell blender with rotation about its axis at 15-25 RPM. This type of blender provides efficient mixing of powders and has proven its utility for many years in the pharmaceutical industry.

Step 6:
Stearic Acid and Silicon Dioxide were added to a polyethylene bag and intermixed and then added to the 50 cubic ft. blender.

Step 7:
Powder was blended for 5 minutes and 10 samples from defined locations in the blender were taken for blend uniformity testing.

Step 8:
The blend was discharged into labeled drums.

Step 9:
The yield of the blend was reconciled. The percent yield was to be 95.0-101.0% of the calculated theoretical amount.

3. Tabletting:

The appropriate tablet tooling, dedusters (used to remove any powder adhering to the tablet) and metal detectors (used to detect any metallic contaminants) were selected and equipment cleanliness was verified. The tablet presses (2) were set up to the specified tablet weight, thickness and hardness and the batch was tabletted using the Stokes BB2 45 station presses with double take off. The double take off refers to the operation of the press, in that a tablet is compressed in one half revolution of the die table. Thus, for every revolution, 90 tablets were produced.

4. Packaging:

The appropriate labels were selected, filling equipment set up and tablets were packaged in predetermined configuration (100's, 5000's). Bottles were filled, rayon coil added, induction sealed and capped. Additionally, the 5000 count bottles were weighed. All label and bottle counts were reconciled.

C. **Raw Material and In- Process Testing:**

1. Raw Materials:

All raw materials were tested before incorporation into Digitek. Digoxin was tested to United States Pharmacopoeia (USP) standards. The USP-NF (National Formulary) is a non-governmental official public standards setting authority for prescription and non-prescription drugs, active ingredients and excipients.

In 2002, Amide applied to FDA to input digoxin into Digitek tablets based on the actual assay of digoxin. Previously, digoxin was incorporated at an assumed label potency of 100%. The USP specification for assay is 95-101%. Therefore, to assure that 100% of the labeled amount was incorporated into the batch, a calculation was performed to adjust the input based on the actual assay of a particular lot of digoxin. This request was approved in June 2002 (letter from FDA to Amide- June 12, 2002- response to a prior approval supplement request) and an adjustment for the actual assay was performed on all batches. Calculation and input of active ingredient based

on actual assay is an acceptable process. It reflects that Amide and later Actavis carefully monitored the purity and amount of digoxin incorporated into Digitek tablets.

The remaining ingredients were all tested to National Formulary (NF) standards. Documents I have reviewed indicated that some lots of excipients were tested also by Gibraltar Labs for microbial contamination and all lots were within specifications (Ref: [2]).

2. In- Process Testing:

a. Blend Uniformity: Blend uniformity (BU) sampling and analysis is the process to demonstrate the adequacy of the mixing of powders to ensure uniformity of in process powder blends. This testing was done to be certain that the powder mix being fed to the tablet press was uniform with respect to digoxin.

The FDA (Guidance for Industry- Powder Blends and Finished Dosage Units, Draft Guidance, October, 2003) has described a process for sampling and testing powder blends to ensure a uniform distribution of ingredients throughout the blend and subsequently uniformity of the finished dose form; in this case, tablets.

This process recommends taking samples from at least 10 locations in a blender representing all areas of the blender. For example, in tumble blenders such as "V" and double cone, samples should be selected from at least 2 depths along the axis of the blender. At least 3 replicate samples should be taken from each location. Typically, the sample size is 1-3X weight of the finished dose form. This is the process that was followed in the blending and sampling of Digitek.

The process is as follows:
-One sample from each location is assayed.
-The Relative Standard Deviation (RSD) for all results is calculated and this should be less than or equal to 5.0%
-All individual results should be within 90-110% of target. Before 2005 (for Actavis) the specification was 85-115%.
-If samples do not meet these criteria, then an investigation should be performed in an effort to determine the cause for the non acceptable results.

In reviewing the Digitek in-process testing for blend uniformity, I noted that 10 locations from defined areas of the 50 cubic ft. blender were sampled. Triplicate samples were obtained ranging from 1-3X tablet weight. The entire sample was sent for analysis, so as to minimize inconsistencies in transfer and preparation of the sample. This process of sample collection (number of samples taken, location where samples were collected, weight of samples, handling) is in conformity with the FDA Draft Guidance. It is worthwhile to note, that between 2003-2007 there were only 4 instances of blend uniformity issues in 470 batches of Digitek manufactured.

There may be instances where out of specification (OOS) results occur when sampling and testing powder blends. These may be a result of non-uniformity of the blend, the type of device used to obtain the samples, the technique used in obtaining the sample, particle size variation of the sample, transferring the sample for analysis, analytical issues including sample preparation, instrument issues and possible analyst error.

There are various types of equipment that can be used to obtain a powder blend sample. Typically, a "thief" with preset cavities is inserted into the powder bed to obtain a sample. Also, a device which produces slugs may be utilized. In an effort to reduce variation and errors in obtaining and transferring samples, the entire sample is analyzed. However, even with precautions in place, there may be instances where OOS results are obtained. This will prompt an investigation which may or may not identify the cause of the OOS.

Differences in particle size of the powders in the blend can adversely affect uniformity by powder segregation. Digitek ingredients were quite uniform in particle size and would not be expected to affect blend uniformity as can be seen from the consistently excellent blend uniformity results. This will be addressed in detail in the Process Validation Section.

Sample transfer and preparation can be problematic. Hence, in testing samples for blend uniformity the entire sample was used to reduce this source of variation. High or low values obtained in blend uniformity testing could be attributed to errors in weighing the digoxin that is input into the original blend. However, this was highly unlikely with Digitek as all weighings required a 2 person validation to verify correctness. Also, any errors in digoxin input would likely show up in finished product testing for Content Uniformity (CU), Assay and Dissolution. There have been no instances that suggest erroneous input of digoxin based on these assays.

OOS blend uniformity testing results may also be due to a less then optimal blending process. This was not apparent with Digitek. During 2003-2007, 470 batches of Digitek were produced. I am aware of only 4 instances where OOS results were obtained. It is also possible that a root cause for the OOS will not be identified. This does not invalidate the process or necessarily cause rejection of the lot. Subsequently, after an investigation a second set of samples can be assayed and if found to be satisfactory, can justify the blending operation. In this case, additional finished product testing may be performed.

I reviewed the lots of Digitek that had initial OOS results for blend uniformity. (Ref: [3]). In all instances samples were retested and if found satisfactory the lot was released; if not, the lot was rejected.

Lot 60992A- One sample out of 10 had an OOS for blend uniformity. Repeat testing was performed and was satisfactory. In addition, content uniformity testing on tablets

from the beginning, middle and end of the batch was satisfactory. The batch was released. I agree with this process.

Lot 70148A- This lot had one OOS value of 87.9% for BU. Repeat testing on a second set of samples was satisfactory. Upon additional finished product testing, the batch was rejected. One group of 10 tablets (of 30 tested) failed CU. This indicated that satisfactory procedures were in place to discover any product that might not meet complete finished product specifications

Lot 70207A- One sample out of 10 tested had a value of 87.3%. Upon review of the batch records and analytical data by staff, no assignable cause was determined. An additional set of 10 samples was assayed and all results were satisfactory. In addition, 30 additional finished tablets were assayed from the beginning, middle and end of the batch. This indicated diligence on the part of Actavis. All data was satisfactory and the batch was released. This was an acceptable process and I agree with this approach.

Lot 70770A- One blend sample out of 10 had a value of 67.9%. Investigation of all data records could not find an assignable cause. An additional set of 10 samples was assayed and all results were satisfactory. In addition, the third set of BU samples was assayed and all results were satisfactory. This demonstrated that the blend was indeed uniform and the blend was released for tabletting. Finished product testing was satisfactory. In my opinion, this was acceptable.

Based on my experience, it is not uncommon that an assignable or root cause relating to OOS results for blend uniformity cannot be found. After an appropriate review of all records, and subsequent additional test results being acceptable, a batch may be released.

In addition, I reviewed the following batch records (Ref: [3]):

60777A, 60994A, 60371A, 70025A, 70454A, 70559A, 70836A, 80002A, 80202A
No deviation or OOS was found relating to BU testing, indicating that the blending process for Digitek was robust, and can be relied upon to produce uniform product.

Additional blend uniformity data was reviewed for the years 2003-2008 (Ref: [4]).

2003, 2004, and 2005: There were no investigations and all analytical data was within specifications, indicating the process was in control.

2006: Except for one lot, 60992A (discussed above) all data was acceptable.

2007: One lot, 70148A, discussed above was rejected. This appears to be the only lot rejected for poor blend uniformity from the 470 produced between 2003-2007.

In addition, I reviewed the following batches made immediately prior to and immediately following Lot 70924A; Lot 70836A and Lot 70925A respectively. (Ref: [3]). Both lots proceeded without any deviations. All results for blend uniformity testing were within specifications. All in process and finished product testing was satisfactory.

2008: An OOS for BU was observed for Lot 80226A. The average result for BU was 106.9%, RSD was 12.8% (spec. NMT 5.0%). Upon investigation it was determined that an HPLC instrument malfunction was responsible. The instrument was repaired. Assay of a second set of samples was satisfactory, with a mean value of 98.6%, RSD 1.0%

This in depth discussion of blend uniformity is pertinent for a number of reasons. It demonstrates that if results from testing are satisfactory, the blend can be released for tabletting. If an OOS result is obtained and after an investigation, acceptable data generated, the blend can be released. If an OOS result is obtained, and further testing is not satisfactory, the batch will be rejected. This is an acceptable process that was followed in the manufacture of Digitek.

b. In-Process Tablets: In order to ensure production of Digitek tablets meeting specifications, multiple samples were evaluated during the set up and compression process. The following parameters were evaluated: tablet weight, thickness, hardness and appearance.

Machine set up: 45 individual tablets from the front take off and 45 tablets from the rear take off for each press were checked individually for weight, thickness and hardness (total of 90 tablets). These tablets were discarded. In addition, if the press was stopped for any reason other than routine breaks, such as punch cleaning, then the set up process was repeated. This was the situation with Lot 70924A where one press was stopped to clean the punches.

During the compression cycle, for the batches I reviewed, the following parameters were monitored by QA every hour from both the front and rear exit chutes:

Individual weight-10 tablets.
Individual thickness-5 tablets.
Individual hardness-5 tablets.
Physical appearance of tablets, for color, shape, size.

In addition, the operators checked the following every half hour from both the front and rear exit chutes:

Total weight and appearance-10 tablets.
Individual thickness-3 tablets.
Individual hardness-3 tablets.

No out of specification tablets were observed during in process testing. This sampling plan was satisfactory and consistent with industry practices.

D. Finished Product Testing:

Before product was released, every batch of tablets was tested to ensure all specifications as detailed in the approved ANDA were met. These tests included:

Product Description: This test ensures the physical description of the tablets meets the specification. For Digitek, the specification was a round bisected tablet either yellow (.125mg.) or white (.250mg.), with the appropriate markings. All released lots pass.

Friability: This is a measure of the fragility of Digitek. This test subjects tablets to the combined effects of abrasion and shock by utilizing a chamber that revolves at 25 RPM and dropping the tablets 6" with each revolution. To meet the specification, not more than 1% tablet weight can be lost. All released lots pass.

Assay: This test determines the amount of digoxin in the tablet. The USP specification is 90-105% of label amount. A composite sample of 70 tablets was collected, ground and a portion assayed. For all the lots I have reviewed, all data was satisfactory

Content Uniformity: This test measures the variability of the active ingredient level in a dosage form. Consistent with USP specifications 10 individual tablets were assayed. Samples met specifications if the acceptance value (AV) was less than or equal to 15%. All released lots pass.

Dissolution: This is a laboratory test to measure the rate of drug release. The USP specification is not less than (NLT) 80% released in 60 minutes. All lots reviewed pass.

Related Substances: This is a test to measure the level of any impurities that may be present in the active ingredient. Specifications for substances other than digoxin include: digoxigenin, digoxigenin bisdigitoxoside, which should not be more than (NMT) 2% each and gitoxin NMT 3%. Typically, less than 1% total was found and results therefore were within specifications.

My review of multiple lots of Digitek and the results of Finished Product testing indicate a robust process of manufacture and a consistent high level of satisfactory results.

E. Process Validation:

Process Validation (PV) is defined as the collection and evaluation of data from the process design stage through production. This process establishes scientific evidence that a process is capable of consistently delivering quality products that meet established specifications.

Validation of a manufacturing process is required before a product approved by the FDA can be commercially distributed.

Typically, 3 lots of product are manufactured to establish a process has been validated. Initially, 3 lots of each strength of Digitek were produced.

Process validation for Digitek was performed in 1994-1996 for the .125mg. tablet (1.6 million tablet batch) and in 1994 for the .250mg. tablet (4.2 million tablet batch) (Ref: [5]).

Process Capability (Cp) is a measure of the ability of a process to produce material that is within the specification range. It verifies that the entire distribution curve for the collected data is within the allowable limits. A value equal to or greater than 1 is acceptable. The process validation evaluated the following parameters:

Parameter	**Combined (.125mg)**	**Cp**	**Combined (.250mg)**	**Cp**
Blend Assay (%)	98.5	2.9	101	4.7
Weight (mg.)	105	1.5	120	1.2
Hardness (Kp)	4.5	2.2	5.1	2.1
Thickness (mm)	2.62	5.7	3.13	6.6
Friability (%)	0.08	.03 (SD)*	0.1	.04
Disintegration (min.)	3.3	.5 (SD)	2.8	.6
Content Uniformity (%)	101	3.2	100.3	3.1
Dissolution (%) 15 min.	83.1	2.7 (SD)	80.3	3.3
60 min.	98.0	3.1 (SD)	95.2	4.0

* Standard Deviation

Critical parameters, such as blend uniformity have been evaluated in the PV trials. As noted in the table above, results obtained were excellent.

In addition, in 1995, tablet press speeds from 14-28 RPM were evaluated in a PV protocol addendum for the .125mg. tablet. Satisfactory tablets were produced at all speeds. Production is typically run at 22-23 RPM.

In 1996, process validation for the .125mg. tablet was performed at a batch size of 4.8 million tablets (2 batches). Blend uniformity testing was performed on each of the 3 individual parts that went into the final blend, as well as the final blend made in the 50 cubic ft. blender. Data for the individual parts were satisfactory and the final blend data (50 cubic ft. blender, mean of 13 samples) were 99.8%, 99.3% with RSD of 1.9%, 3.5% respectively.

Particle size data from top, middle and bottom of the final blend was similar for both batches. Values for weight, hardness, thickness, content uniformity, dissolution and friability were all within protocol specifications and comparable to the 1.6 million tablet batch size.

These data support the conclusion that the process for the manufacture of Digitek was validated and that all processes were in control (as indicated by Cp values) and thus would be expected to yield consistently satisfactory product.

Upon review of the Process Validation data for Digitek and in depth review of batch records of multiple lots including lots made between 2003-2008, I concluded that the Digitek manufacturing process was developed based on established pharmaceutical science principles. The multiple batches reviewed also indicated that the manufacturing process was in control and capable of producing satisfactory tablets.

F. Annual Product Reviews:

The Annual Product Review (APR) is a summary of all batches made of a particular product for a specific year. It summarizes all critical parameters of a product such as BU, assay, CU, weight, thickness, hardness, friability, dissolution and batch yield. It also reviews any deviations (planned or unplanned), investigations, etc. It is also important to review trend data as this demonstrates the uniformity (or lack) of the process and whether the process is statistically in control.

I have reviewed the APR's for 2003-2008. My conclusion is that for Digitek, the data discussed below demonstrated a well controlled manufacturing process.

2003: 56 batches of .125mg. and 55 batches of .250 mg. were produced. All data, such as blend uniformity, assay, content uniformity, dissolution, thickness and hardness were within specifications and satisfactory.

2004: 42 batches of .125mg. and 35 batches of .250 mg. were produced. All data were satisfactory. For batch 3611A, a pharmacist noticed a single tablet with greater than normal thickness. The tablet was returned and confirmed to be Digitek. Upon investigation, it was postulated that the tablet remained in the deduster during the start up procedure and was not discarded prior to routine production. This was an extremely rare occurrence. The operators were informed to ensure no tablets remain in the deduster prior to production.

2005: 53 batches of .125mg. and 47 batches of .250 mg. were produced. All data were satisfactory. There was one customer complaint related to a .125mg tablet. It appeared that a metal shard (like a staple) was adhering to the surface of the tablet. An investigation determined that this did not occur in the plant.

2006: 50 batches of .125mg. and 44 batches of .250mg. were produced. All data for all parameters tested were satisfactory.

2007: 54 batches of .125mg. and 34 batches of .250mg. were produced. As previously noted, Batch 70148A had an OOS result for BU. Upon retest of a second set of samples, all passed. The batch was rejected when one set of 10 tablets (of a total of 30) tested for content uniformity failed with an Acceptance Value (AV) of 18% (Specification NMT 15%) and a mean value of 105.9%.

Lot 70924A: (Ref: [1,4]). This lot was manufactured in November 2007. All in process testing (weight, hardness, and thickness) was satisfactory. One of 2 tablet presses was stopped during the run to remove excess powder build up from the punches. It was then restarted after going through a complete restart procedure. Powder build up is not uncommon and interrupting production to clean tooling is acceptable. All in process data was satisfactory. As an example, the BU testing yielded values of 96.4-101.1%, a mean value of 98.6% and an RSD of 1.8%, demonstrating excellent BU. Finished product testing yielded results that were all within specifications.

It was noted during packaging that 5 tablets had thickness greater than specifications. The entire batch was then subjected to 100% visual inspection and a total of 20 tablets were identified as OOS for thickness. The tablets were removed from the batch. Subsequently, a tightened Acceptable Quality Limit (AQL) inspection was performed on an additional 1330 tablets and no additional thick tablets were found. The batch was packaged and released.

No root cause for the thick tablets was identified. It is possible that the tablet deduster which was in place during the start up and weight adjustment process had trapped some of these tablets as routine production began and were subsequently collected. The operators were instructed not to place the deduster in line until after set up was complete.

It is important to note that even though this batch was released and subsequently recalled at FDA's request, there was no report of any double thick tablet from this batch being found by a pharmacist or patient.

In my opinion, the processing and investigation that was performed, including acceptable BU, in process weight checks, thickness and hardness checks and finished product testing were all within acceptable procedures. The additional 100% inspection and tightened Acceptable Quality Limit testing was adequate for batch

release with the assurance that no tablet with out of specification thickness would be released.

2008: 19 batches of .125mg. were produced. One lot 80228A was rejected for overweight tablets found during packaging. The remaining lots were recalled as per FDA agreement.

G. Stability Studies:

All marketed product is required to have ongoing stability studies on a yearly basis, even when an expiry date has been previously established. The purpose of a marketed product stability program is to constantly reconfirm that the product can be expected to remain within specification throughout its labeled shelf life.

I have reviewed Digitek stability data for numerous lots in all packaging configurations, including Digitek packaged by UDL in blisters. Stability testing included tablet appearance, assay for potency, related substances and dissolution. Many of the studies were carried out for 3 years. Results for all tests were within specifications, demonstrating that Digitek had adequate data to support a 2 year expiry (Ref: [6]).

H. Summary of UDL/Mylan Testing:

UDL Laboratories packaged Digitek tablets in individual blisters. At the request of UDL, Celsis Laboratories tested batches of Digitek for assay and dissolution. (Ref:[7]). Lots 61100A, 61097A and 60992A (bottles of 100's from Mylan) were tested and initial results of bottled samples met all specifications.

In reviewing the data for both strengths of Digitek (See Memo: Sue Powers from Tom Spraine 5/5/08; Stability Review of Digitek .125mg. and .250mg. tablets, Defendant's Exhibit 84) UDL had product tested for potency and dissolution. All data was within specification. Overall, both strengths showed "no remarkable stability data through the assigned expiration in the unit dose package." UDL also had 6 stability studies ongoing in May, 2008. All data leading up to that time was satisfactory.

In addition, I have reviewed stability data for 31 lots of Digitek packaged by UDL from as early as 1999. Storage times up to 36 months were evaluated depending on the lot. All data was satisfactory (Ref: [7]). These results demonstrated the excellent shelf life stability of Digitek tablets.

It is important to note that UDL never found an "oversize" tablet in any of its production packaging runs. In fact a "double thick" tablet would not have fit within either the .125mg. blister cavity or the .250mg. blister cavity. UDL specifications for

tablet thickness (2.58-2.98mm for the .125mg, and 3.15-3.29mm for the .250mg. tablet) are tighter than Actavis' (2-3mm for the .125mg. and 2.7-3.7mm for the .250mg.). A blister has only an excess headspace of 10% of the maximum UDL thickness specification for Digitek tablets. Thus, for a .125mg. tablet, the maximum thickness that would fit in the blister was 3.28mm and for .250mg. tablet the maximum thickness was 3.62mm. Neither of these dimensions are close to a "double thick" tablet. This again demonstrated the Digitek process was under control.

I. FDA Sampling:

FDA routinely collects commercial samples of products for testing in its laboratories as part of its "484" program. This program is ongoing and is another process to validate that marketed product meets all regulatory specifications. Multiple samples of Digitek were collected by FDA inspectors from commercial sources (pharmacies) and from the manufacturer. The following lots were reviewed: 8A332 (.25mg. blisters), 7P964 (.125mg. blisters), 70078A1 (.125mg.), 70737A1 (.125mg.), 706641A1 (.250 mg.), 70811A1 (.250mg.), 70298A1 (.125mg.). Also, FDA Collection ID's: 157504 (.125mg.), 178890 (.125mg.), 178891 (.125mg.), 157503 (.125mg.). The following tests were performed: Content Uniformity, Identification and Dissolution. All samples tested passed. This is yet another example of the quality of manufactured product. As stated in the FDA reports "samples were compliant".

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J. Review of FDA Correspondence:

FDA inspects pharmaceutical plants on a regular basis. An inspection may involve a tour of the plant, review of documents such as batch records, analytical results, laboratory notebooks, policies and procedures, etc. Comments noted by the inspector are recorded on FDA Form 483, which is presented to the firm upon completion of the inspection. These comments may relate to variation in processes, instances where the inspector may find discrepancies regarding process issues and even a misplaced signature in a notebook or a missing date can be noted.

The issuance of a 483 does not, a priori indicate manufacture of a faulty product or a breakdown in procedures.

I have reviewed the following FDA correspondence:

483- 1/10/06-2/8/06: These observations related mostly to timing of reporting of Adverse Drug Events (ADE's) and consumer complaints. There were 3 observations regarding manufacturing issues not related to Digitek.

Warning Letter- 8/15/06: This related to inspection of 1/10-2/8/06 and ADE reporting, not manufacturing issues.

483- 7/10/06-8/10/06: The observations related to the investigation of some laboratory procedures. There were also observations regarding cleaning validation for Digitek, in that sample recovery was performed on swabs rather than after application to a coupon.

Warning Letter- 1/9/07, updated 2/2/07: This letter related to the inspection of 7/10/06-8/10/06 and requested Actavis to retain a third party to review procedures. Quantic Regulatory Services (QRS) was hired to perform the review.

QRS is well known in the pharmaceutical industry and performs prospective and retrospective reviews on all phases of manufacturing. Their reports are detailed and in my experience their evaluation of processes and procedures are accepted and well received by FDA. QRS reviewed records of a total of 39 batches of Digitek (.125mg. and .250mg.) manufactured during 2005-2006. They reviewed deviations, investigations and instances of OOS data.

Their conclusion stated that the review "did not contain non conformances or deficiencies that were likely to have had a material adverse impact on the identity, strength, quality or purity of batches reviewed." These comments were submitted to FDA which did not reject them. This was a strong statement by QRS which indicated that adequate procedures were in place for the manufacture, packaging and release of Digitek.

483- 3/18/08-5/20/08: One observation referred to Lot 70924A and stated that "double thick" tablets were found and no root cause was determined. The observation indicated that the batch was released upon visual inspection of 1330 tablets. It should be noted that the entire batch was visually inspected for thick tablets and a total of 20 were found and removed. An additional sample of 1330 tablets was inspected as well. No thick tablets were found in this AQL inspection of 1330 tablets. While no root cause was identified, a viable explanation was postulated that the deduster was in place at the tablet press during machine set up and tablets produced during weight adjustment were trapped in the deduster and were discharged into the batch. Also, it was possible that an initial misalignment of the take off bar could be responsible.

In my opinion, the 100% inspection and additional AQL testing was a valid procedure to eliminate oversize tablets. It is worthwhile to note FDA's comment on this issue (Ref: [34]): "In our best judgment, given the very small number of defective tablets that may have reached the market and the lack of reported adverse events before the recall, harm to patients was very unlikely."

Another observation related to OOS results for some blend uniformity samples (Lots: 70148A, 70207A, 70770A) and lack of manufacturing investigation. QA evaluated the data and found no root cause in the analytical review. Additional samples were

analyzed and lots 70207A and 70770A were released based on acceptable results. Lot 70148A which demonstrated acceptable BU data upon retest, was not released based on some unacceptable content uniformity testing of the finished product. In my opinion, these were valid procedures. Issues and difficulties related to blend uniformity testing are discussed in detail in Section 2.a.

A product(s) may be declared "adulterated within the meaning of 21 U.S.C. §351(a)(2)(B), Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act) in that the methods used in, or the facilities or controls used for their manufacture, processing, packing or holding do not conform with cGMP's, to assure that such drug products meet the requirements of the Act." It is important to note that there have been no instances demonstrated where any patient received a "double thick tablet" and that no Digitek tablets were released that did not meet all approved specifications.

K. Conclusions:

My in-depth review of Digitek documents supplied to me leads me to the following conclusions supported in part by my more than 35 years experience in the pharmaceutical industry.

1. The process for manufacturing Digitek tablets by direct compression was robust and that this process is commonly used throughout the pharmaceutical industry.

2. Process validation of Digitek demonstrated a well designed manufacturing process with an acceptable Cp.

3.. The inert ingredients used are common pharmaceutical excipients.

4. The manufacturing batch record was well written and detailed. Processing steps were logical and resulted in satisfactory product.

5. Equipment was standard and fully suited to the manufacture of Digitek.

6. In-process testing was adequate to ensure satisfactory product.

7. Finished product testing conformed to the ANDA.

8. Annual product reviews for 2003-2008 as well as numerous batch records evaluated demonstrated that the process was in control.

9. All stability studies of Digitek produced results to support the labeled expiry.

10. Numerous commercial samples collected and analyzed by FDA have shown all results to be within specification.

11. Instances of OOS data for some in process tests have been adequately investigated and rational decisions made.

12. The diligence of the staff was good, as noted when oversize tablets were found during packaging and removed from the batch.

13. FDA found no instances of low or high content Digitek tablets leaving the plant.

14. There have been no instances, of which I am aware where a patient has received anything other than a Digitek tablet with the correct amount of labeled ingredient.

15. Celsis testing of Digitek, on behalf of UDL has consistently produced results that showed product was in specification.

16. I am confident, based on my review that the formulation, processing, testing and packaging was satisfactory to ensure that Digitek tablets that have been marketed were fully within approved ANDA and USP specifications.

Respectfully submitted,

Lewis P. Amsel, Ph.D.
December 9, 2010

APPENDIX: DOCUMENTS REVIEWED

1. Batch 70924A, manufacturing records, in process and finished product testing ACTAV 2112-3336.

2. Gibraltar Labs., Results of micro testing of excipients, 9/6/05-4/15/08.

3. Batch Records and Finished Product Testing of Lots: 60777A, 60994A, 60371A 70025A, 70454A, 70559A, 70670A, 80002A, 80202A, 70207A, 70770A, 70836A, 70925A, 80226A, 80228A, 70148A.

4. Digitek Annual Reviews 2003-2008.

5. Process Validation Reports, .125mg, and .250mg.

6. Actavis Stability Data Reports: Lots: 60319A, 70023A, 70078A, 70081A, 70174A, 70176A, 70670A, 71049A, 71051A.

7. UDL Stability and Test Data; 34 lots 1999-2008. Exhibit 83 (UDLL 11361-11401, UDLL 11679-11769, UDLL 4768-4771).

8. Deposition of A. Delicato, 5/28/09.

9. FDA Form 484, 4/16/03

10. Deposition of L. Radke, 1/26/10.

11. UDL organization charts, memos. Deposition of L. Radke.

12. UDL test results, lots: 80111A, 71034A, 71004A, 70770A, 70175A, (UDLL 5805-5815, UDLL 7647-7698).

13. L. Radke: Warning Letter summary, 2/10/07.

14. Celsis testing document, lots: 61100A, 5A113, 61097A, 60992A.

15. Correspondence between Actavis and FDA, 12/24/07.

16. Correspondence between QRS and Actavis regarding retrospective batch review, 5/17/07, 12/21/07.

17. Documents regarding recall, Actavis, Mylan. Plaintiff's Exhibits 107, 125, 138. ACTAV 313948-313950.

18. Documents discussing the finding by a pharmacist of an "extra thick" tablet, 7/7/04. Plaintiff's Exhibits 128, Doc. ID 73319.

19. Correspondence between Actavis and FDA, 11/6/06. ACTAV 28850-28860, redacted response to 10/11/06 Form 483.

20. Response to Form 483, 8/29/06. ACTAV 28958-28999.

21. Cleaning Validation Master Plan, 6/14/07. Doc. ID 72795.

22. Correspondence between Actavis and FDA, compliance update, 3/5/07. Doc. ID 144053.

23. QSIP update, 12/5/06. Doc. ID 182316, 75911.

24. Investigation of blend uniformity failures, 2007. ACTAV 165623-165630, Exhibit 183.

25. Investigation of Lot 80051A for oil spots, 2/5/08. Plaintiff's Exhibit 129.

26. Investigation of Lot 80228A. Plaintiff's Exhibit 141, 142.

27. FDA Prior Approval Letter for digoxin calculation, 6/12/02.

28. Plaintiff's General Liability Expert Reports, 6/18/10.

29. FDA Form 484 samples testing and results. (464753, 462746, 377410, 453913, 448892, 454866, 157503, 157504, 178891, 178890).

30. Letter to Amide from FDA, certification for batch release, 6/8/95.

31. e mail: L. Farrell reports finding a card with digoxin containing one "double thick" tablet. MYLN 932682-932683.

32. List of Digitek batches recalled, 5/20/10. Prepared by S. Wamelink.

33. Actavis' SOP's, 0016, 0017, 0019, 0033, 0055.

34. FDA, Health News Digest.com, Fact and Myths about Generic Drugs, July 8, 2009.